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REMARKSInterview Summary

Applicant's Attorney and Agent, Steven Davis and Michael Gottselig, would like to thank the Examiner and Supervisory Examiner for conducting the telephonic interview of November 30, 2006. During the interview the following points were discussed:

- A) the rejections under 35 U.S.C. §112 of record, based on (1) indefiniteness of claim language and (2) double patenting, were discussed;
- B) the rejections under 35 U.S.C. §102 of record, based on Sneddon et al. (WO 01/87849), were discussed.

With regard to A) (1), the Examiners agreed that the introduction of the list of substituents from the specification page 9, line 10 through page 10, line 12 into Claims 1, 2 and 26 would overcome the rejections based on 35 U.S.C. §112.

With regard to A) (2), the Examiners agreed that Applicants address the provisional double patenting rejection of Claims 1-26 in the subject application if the corresponding claims of co-pending U.S. Patent Application No. 10/719,701 are allowed or patented before the claims of the subject application, and, if this provisional double patenting rejection is the only rejection remaining in either the subject application or co-pending Application No. 10/719,701 after entry and consideration of any Amendments, that the rejection would be withdrawn and either the subject application or co-pending Application No. 10/719,701 permitted to issue as a patent, in accordance with U.S. Patent Office procedure (see, M.P.E.P. § 804(I)(B)(1)).

With regard to B), the discussions focused on whether Graft Versus Host Disease (GVHD) is encompassed by the term "transplant rejection." The Examiners agreed that further submission of exhibits evidencing that GVHD is not encompassed by the term "transplant rejection" would be considered and could overcome the rejections. Examiner also suggested that amending the Claims to clearly exclude GVHD from the alleged scope of the Claim could overcome the rejection.

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Claim Amendments

Claims 1, 2, 24, 25 and 26 have been amended to further clarify that these Claims are directed towards inhibiting transplant rejection and not GVHD as discussed below. Claims 1, 2 and 26 have further been amended to define the list of substituents as discussed below.

Claims 11, 12 and 17 have been amended to correct clerical mistakes. In Claims 11 and 17 an "is" has been inserted. Claim 12 contained the phrase "an optionally substituted" twice in consecutive order. Accordingly, Claim 12 has been amended to delete "an optionally substituted."

No new matter has been added as a result of these amendments.

Clerical Mistake in Reply to Office Action filed February 28, 2006

Applicants stated in the last two lines of page 5 of Applicants' Reply filed on February 28, 2006 that "graft versus host disease (GVHD) is not a typical host rejection of a tissue transplant". In fact, GVHD is not a host rejection at all. Any interpretation to the contrary was not intended.

Claim Rejection under 35 USC § 112

Claims 1-4 are rejected under 35 USC § 112 second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner asserts that Claims 1-4 are indefinite because the variables represented by the R groups do not list all possible substituents which are included in the terms "substituted or unsubstituted".

Applicants have amended Claims 1, 2 and 26 to include a list of substituents. Support for this amendment can be found in the specification, page 9, line 10 through page 10, line 12. Because Claims 3 and 4 depend from Claim 2, the inclusion of substituents in Claim 2 also overcomes the rejections of Claims 3 and 4. No new matter is added as a result of these amendments.

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Provisional Claim Rejection under the judicially created doctrine of Double Patenting

In the Office Action of October 31, 2005, the Examiner provisionally rejected Claims 1-26 under the judicially created doctrine of double patenting over Claims 1-20 of co-pending Application No. 10/719,701. The Examiner has maintained this rejection

Applicants will address the Double Patenting Rejection once the Examiner indicates that the Claims of the application are otherwise in condition for allowance.

Claim Rejection under 35 USC § 102 (b)

Claims 1-26 are rejected under 35 USC § 102(b) as being anticipated by Sneddon *et al.*, WO 01/87849.

In making this rejection the Examiner states that Sneddon *et al.*, teach a method of inhibiting tissue transplant as graft versus host disease (GVHD) and refers to page 14 line 30 of Sneddon *et al.*

In the telephone interview with the Examiners, the Examiners stated that further submission of exhibits evidencing that GVHD is not encompassed by the term "transplant rejection" would be considered and could overcome the rejections. Examiner also suggested that amending the Claims to clearly exclude GVHD from the alleged scope of the Claim could overcome the rejection.

Following the Examiners' suggestion, Applicant amended the preambles of Claims 1, 2 and 24 to 26 to clarify that GVHD is not encompassed by the Claims. Support for these amendments can be found, for example, on page 6, lines 12 to 20. Applicant submits that these amendments merely clarify but do not narrow the scope of the Claims. For example, the preamble of Claim 1 has been amended as follows:

A method of inhibiting rejection of a transplanted organ, tissue or cell in a subject ~~tissue transplant rejection in a subject with a tissue transplant,~~

...

The recitation of "rejection of a transplanted" as compared to "transplant rejection" clarifies that it is the host that rejects the graft. As will be discussed below, the reverse is true for GVHD

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(Graft Versus Host Disease), in which the graft rejects the host. The same change in claim language has been introduced with the amendments of Claims 2 and 24 to 26.

Furthermore, following the Examiners' suggestion, Applicant provides documentation from three text books showing that a person having ordinary skill in the art understands GVHD not to be encompassed by either "transplant rejection" or "rejection of a transplanted organ," etc. and *vice versa* as discussed in the following.

Harrison's Principles of Internal Medicine, 15<sup>th</sup> Edition, edited by E. Braunwald, A.S. Fauci, D.L. Kasper, S.L. Hauser, D.L. Longo and J.L. Jameson, McGraw-Hill, 2001, states with respect to a bone marrow transplant on page 739, right-hand column, first full paragraph (see Exhibit A):

Following allogeneic transplantation immune cells transplanted with the marrow or developing from it can react against the patient, causing GVHD. Alternatively, if the immunosuppressive preparative regimen used to treat the patient before transplant is inadequate, immunocompetent cells of the patient can cause graft rejection. (Emphasis added)

This statement clearly states that 1) GVHD is caused by the graft reacting against the patient, 2) graft (or transplant) rejection is caused by cells of the patient, and 3) GVHD is not understood in the art to be encompassed by the term graft (or transplant) rejection and *vice versa*, as emphasized by the recitation of "alternatively."

Further support that a person having ordinary skill in the art does not understand GVHD to be encompassed by graft (or transplant) rejection and *vice versa* is provided in the first sentence in the fourth paragraph on page 739, right-hand column:

With current techniques, the risk of graft rejection is 1 to 3%, and the risk of severe, life-threatening acute GVHD is approximately 15% following transplantation between HLA-identical siblings. (Emphasis added)

Again, GVHD and graft (or transplant) rejection are treated as two distinct conditions.

Further support that a person having ordinary skill in the art does not consider GVHD to be encompassed by graft (or transplant) rejection and *vice versa* is also provided in other

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references, for example, Immunobiology, 5th Edition, edited by Charles A. Janeway, Paul Travers, Mark Walport, Mark Shlomchik, Garland Publishing, 2001 (see Exhibit B) and Clinical Laboratory Medicine, Edited by K. D. McClatchey, Williams & Wilkins, 1994 (see Exhibit C).

With regard to Exhibit B, GVHD and graft (or transplant) rejection are treated in two different sections, Section 12-21 and Section 13-22, respectively, evidencing that GVHD and graft (or transplant) rejection are considered distinct and different conditions. Furthermore, the section title of Section 13-21 reads "[t]he converse of graft rejection is graft-versus-host-disease." Thus, clearly, GVHD is not considered to be encompassed by graft (or transplant) rejection.

With regard to Exhibit C, page 808, right-hand column, first paragraph of the section "Transplantation – Bone Marrow" states:

In patients who have never been previously immunized to HLA antigens, the single most important consideration in the grafting of bone marrow is the prevention of a reaction of the engrafted cells against the recipient. Immunologically competent donor cells reacting with recipient tissues can lead to serious disorder known as graft versus host disease (GVH). Most patients who require a bone marrow transplant have a nonfunctioning immune system because of their underlying disease or therapy. If this is not the case, deliberate immunologic incompetence is induced by cytoreductive chemotherapy and/or irradiation prior to transplantation. Under these conditions, the recipient cannot respond easily to foreign antigens in the donor and therefore the problem of graft rejection is not as important as in other forms of transplantation. (Emphasis added)

Again, this statement clearly states that 1) GVHD is caused by the graft (engrafted cells) reacting against the patient, 2) graft (or transplant) rejection is caused by the response of patient's immune system against the graft, and 3) GVHD is not understood in the art to be encompassed by the term graft (or transplant) rejection and *vice versa*. The latter is made very clear by referring to GVHD as the "single most important consideration" in the grafting of bone marrow and the problem of graft (or transplant) rejection as "not as important."

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With respect to all of these exhibits, it is particularly noteworthy that the verb "reject" and the noun "rejection" is never used in reference to GVHD. Instead, for example, the words "complication" or "GVH reaction" are used.

In conclusion, the passages quoted above from textbooks in internal medicine, immunology and clinical laboratory medicine evidence that GVHD and graft (or transplant) rejection are known in the art to be fundamentally different. Further, these two terms are not considered to overlap in scope, that is, it is well understood in the art that if one speaks of "transplant rejection" or "rejection of a transplanted" organ, tissue or cell, one does not speak of GVHD. Accordingly, methods of inhibiting "transplant rejection" or "rejection of a transplanted" organ etc. are not anticipated by Sneddon *et al.* who teach treating GVHD.

Therefore, the amended Claims 1-26 are novel and patentable in light of Sneddon *et al.*, and withdrawal of the rejection is respectfully requested.

### CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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